REVIEW

Head and Neck Cancer: Global Burden and Regional Trends in India

Anupam Mishra[1]*, Rohit Meherotra[2]

Abstract

The actual burden of head and neck cancer in India is much greater than reflected through the existing literature and hence can be regarded as a 'tip of iceberg' situation. This has further been evident by the recent reports of 'Net-based Atlas of Cancer in India'. South-east Asia is likely to face sharp increases of over 75% in the number of cancer deaths in 2020 as compared to 2000. Since the percentage increase of Indian population has been nearly twice that of the world in last 15 years there is a likelihood of increase in cancer burden with the same proportion. The distribution of population based cancer registries is grossly uneven with certain important parts of the country being not represented at all and hence the current cancer burden is not reflected by registry data. However, the pathetic situation of health care system in major parts of the country as also emphasized by the World Bank, is not suitable to provide anywhere near accurate data on cancer burden. Head and neck cancer (including thyroid lesions) is third most common malignancy seen in both the sexes across the globe but is the commonest malignancy encountered in Indian males. Also oral cavity cancer is the most prevalent type amongst the males and one of the highest across the globe. This article reviews the latest global and national situation with an especial emphasis on head and neck cancer. Furthermore this review focuses on burden in different sub sites at national and global levels.

Keywords: Cancer - lip - tongue - oral cavity - oropharynx - nasopharynx - hypopharynx - larynx - thyroid - India

Asian Pac J Cancer Prev, **15 (2)**, 537-550

Cancer in India: Global Perspective

The total burden of cancer across the globe is estimated to be around 22 million (WHO-UICC 2003). Approximately 10 million new cases of cancer are diagnosed every year across the globe (WHO-UICC 2003). The cancer incidence of the world in terms of income as per the world bank data is briefly depicted in Table 1. It is evident that more than 5 billion people (85% of the world's population) reside in developing countries that account for only 20% of the global gross national product2. Hence the great majority of new cases (more than 60%) are from the developing world including India. Cancers in all forms are causing about 12% deaths throughout the world (WHO-UICC 2003). In developed country cancer is the second leading cause of death accounting for 21% (2.5 million) of all mortality. In developing countries cancer ranks third as a cause of death and accounts for 9.5 % (3.8 million) of all deaths (NCCP 2006). It is estimated that by the end of the year 2020 over 10 million people world wide would die of cancer every year (WHO-UICC 2003) and that 66% of these would be from the newly industrialized and the developing world (WHO 2003). WHO has categorically stated that in 2020, regions with traditionally low numbers of cancer deaths could see alarming increases in the mortality rates (WHO 2003). Regions including northern Africa, western Asia, south America, the Caribbean and south east Asia would face sharp increases of over 75% in the number of cancer deaths in 2020 as compared to 2000. India being a major contributor to population explosion is likely to run a great risk of producing cancer burden. Table 2 depicts that within last 15 years the percentage increase of Indian population is twice that of the world and has supposedly contributed to maximum population growth across the lower or the middle income countries. Cancer pattern varies not only through out the world but also between different populations groups within the same country. In general the more common cancers in males across the globe in order of prevalence are that of the lung and prostrate while those in females are that of breast and uterus. Therefore the cancer of head and neck (including thyroid) follows next as the third common malignancy seen in both the sexes across the globe.

As mentioned before the majority of the total world population resides in the developing countries especially

Table 1. Relative Economies of the Countries

Economies*	Total No. of countries*	Countries with available data on cancer incidence NO.	Percentage of total
Low income	61	15	24.59
Lower middle income	56	19	33.92
Upper middle income	37	14	37.83
High income	54	28	51.85

*Data and Statistics of the World Bank Group

[1]*Department of Otolaryngology and Head and Neck KG Medical University Lucknow,* [2]*Rama Medical College, Mandhana Kanpur, India* *For correspondence: amishra_ent@yahoo.com

in Africa and Asia. The cancer registries in the developed nations give a better reflection of cancer burden as compared to that of the underdeveloped countries. Table 3 depicts the continental distribution of cancer registries across the globe. Despite the fact that the burden of cancer is higher in the developing world, it may still be considered just as 'a tip of iceberg', masking the true incidence. Noteworthy those nations with comparatively larger population contributing to the 'population explosion' have a substantial lower number of cancer registries (Table 4). Hence for example in USA with a population density of 0.03 billion per million square kilometers and 0.01 million per cancer registry centre, the cancer load estimation would be better than India/China.

The above discrepancy can further be highlighted with smaller nations like Switzerland. With a population density of 169 persons per square kilometer and 10 cancer registries in its territory, a single cancer registry from Switzerland caters to a population of 700,000 persons and to an area of 41,290 square kilometers (Table 5). In contrast there are 11 registries in India that cater to an entire population of 1.08 billion spread across 3.29 million square kilometers. Hence with a population load of 98 million per registry and that too in a country with such a diversified cultural/economic/social practices, it may be possible to appreciate the changing trends of cancer but quite difficult to estimate the actual burden specially with the same precision as that of the developed nations. Being roughly four times more populated, India as compared to USA would accordingly need about 4 times more number of registries as that of USA. This further emphasizes the 'tip of iceberg' hypothesis for cancer incidence in Indian population and provides a necessity for having more number of evenly distributed cancer registries across the country.

Table 2. Major Population Distribution (in billion) of World, Low and Middle Income Group Countries

		1990	2005	Difference	% increase
World*		5.3	6.5	0.8	15.1
	India	0.84	1.08	0.239	28.5
Countries	China	1.15	1.30		
	India	0.84	1.08		
	Indonesia	0.19	0.24		
	Brazil	0.15	0.18		
	Pakistan	0.11	0.16		
	Bangladesh	0.11	0.14		
	Russia	0.14	0.14		
	Nigeria	0.08	0.12		
	Philippines	0.06	0.08		

*Based on world population clock; US Census Bureau and International data base, US Census Bureau

Table 3. Continental Distribution of Cancer Registries (countries) of the World

	Total No. of Countries Reporting Cancer Data				
Economies*	Asia	Africa	Europe	America	Australia
Low income	5	7	-	-	-
Lower middle income	7	1	3	7	-
Upper middle income	2	-	8	4	-
High income	4	-	18	3	3

*Data and Statistics of the World Bank Group

Table 4. Cancer Registries from the Top Populated Nations

S. No.	Country*	Population in billions (2005)*	Surface area (million square km)	Population density per million sq. km.	No. of cancer registries**	Population density (million) per registry
1	China	1.3	9.5	0.13	10	0.13
2	India	1.08	3.29	0.32	9	0.12
3	USA	0.29	9.6	0.03	20	0.01
4	Indonesia	0.24	2	0.12	Nil	NA
5	Brazil	0.18	0.85	0.21	7	0.02
6	Pakistan	0.16	0.80	0.20	1	0.16
7	Bangladesh	0.14	0.14	1.00	Nil	NA
8	Russia	0.14	17	0.008	1	0.14
9	Nigeria	0.12	0.92	0.13	1	0.12
10	Japan	0.12	0.37	0.32	8	0.01

*Based on International database, US Census Bureau; **IARC - WHO 'Cancer incidence in five continents' vol. VIII (2002)

Cancer in Indian Subcontinent: A National Perspective

Cancer has become one of the ten leading causes of death in India3. Takiar and Vijay (2011) have reported an increase of 55.8% cancer incidence in past 2 decades as per the national urban registries. The data accrued by National Cancer Registry Program (NCRP) reflects only a few selected urban centers with only one rural registry, (covering only a part of the district). Therefore it is difficult to estimate the true burden of cancer of the entire country where more than 70% of the population (of India) resides in rural areas BSAA 2004). None the less limited work has been done (Murthy et al., 1990) in the NCRP, and these figures estimate the number of newly diagnosed cancer to be within 700,000 to 900,000 per year with an annual mortality of 3 lakhs. Since this data is around 15 years old and proper reflection of the rural population has never been achieved till date, the precision of the estimates are just approximate. Nearly 1.5 million patients require facilities for diagnosis, treatment and follow-up at a given time (NCCP). Although the urban population theoretically has the access to tertiary care hospital but the majority of the rural population receive inadequate or no therapy since many never reach treatment centres. However even in such centres, the accumulation of a body of data which would provide a foundation on which to build a better treatment approaches has been hampered by incorrect or incomplete diagnoses, inconsistent treatment and poor documentations of results. Data from population based registries under NCRP indicate that the leading sites of cancer are the oral cavity, lungs,

Table 5. Anticipated Discrepancy of Data Accuracy (quality) Amongst Different Countries

S. No.	Country*	Population (2005)*	Surface area	No. of cancer registries*
1	USA	0.29	9.6 million square Km.	20
2	Canada	0.033	10 million square Km.	15
3	Italy	0.058	301 thousand square Km.	19
4	U.K.	0.06	243 thousand square Km	20
5	Switzerland	0.007	41,290 Km.	10
6	China	1.30	9.5 million square Km.	9
7	India	1.08	3.29 million square Km.	11

oesophagus and stomach amongst men and cervix, breast and oral cavity amongst women. Cancers specially those of oral cavity and lungs in men and cervix and breast in women account for over 50% of all cancer deaths in India (NCCP). In general there are regional differences in rates (ASR) from 87.8 (Trivandrum) to 123.3 (Delhi) in urban males and 81.1 (Trivandrum) to 135.6 (Delhi) in urban females8. The rural registry of Barshi reveals ASR of 4.2 in males and 57.7 in females (NRCP 2001). Owing to different genetic constitution of various ethnic groups and the differences in the exposure of different sectors of population to environmental carcinogenic factors, the pattern of cancer in terms of the annual incidence, relative frequency, and subtypes of different cancers vary markedly amongst population subgroups. India is as such a unique country owing to its extreme diversity in climate and culture. The most common ethnic groups are Indo-Aryan (72%), Dravidian (25%), and mongoloid (2%); while the different religious groups comprise Hindus (81.3%), Muslims (12%), Christians (2.3%), Sikhs (1.9%), others (2.5%) including Buddhists, Jains and Parsis (BSAA 2004). Furthermore there are 18 different official languages spoken in the different parts of the country. Hindus comprising the largest proportion are although classically divided into Brahmins, Khatriyas, Vaishas, and Shudras, but in reality the society in India is divided into thousands of jatis (sects), local endogamous groups, organized hierarchically as per the complex ideas of purity and pollution (BSAA, 2004). Not only this Hindus further believe in several millions of gods/goddesses/faith leaders etc., further dividing them as per the 'whims and fancies'. Such a diversification has a profound impact on the various culture practices that are unique in different parts of the country.

To simplify the discussion the various registries can be divided into different national zones as per Table 6. It is evident that apart from southern regions, the country is not well represented. Compared to 4 population based registries in the southern part of the country, the east, west and north-central areas are represented by a single registry only namely Kolkata, Ahmadabad and Delhi-Bhopal respectively; while the extreme north (Jammu and Kashmir) being not covered by any. These areas have a significantly different subpopulation in terms of culture, religion, practices, beliefs etc. necessitating their consideration. Moreover the only rural registry of Barshi does not justify its representation of 70% of rural Indian population as indicated earlier. It is surprising that due to the reasons unknown the data from this rural registry and that from Bhopal has not been included in the latest world cancer registries of 5 continents. Even the existing data from the above registries also reflect certain limitations in the accuracy of mortality data including the system of registration of death as well as certification of the cause of death. Although in urban centres all deaths are generally registered, information on the exact cause of death is lacking. When cancer is mentioned as a cause, the anatomical site is not mentioned and when site is mentioned the histology and morphology are not stated (NRCP 2001). Because of this there are difficulties in having a clear and complete picture of cancer mortality as opposed to morbidity. Mumbai has comparatively developed a relatively better system mainly because of the earlier coroners act. Data collection, summation, analysis however meticulously performed cannot be ideal. Timeliness has not always been followed and some registries had to subsequently add substantial number of cases of earlier years as 'late registrations'. This reflects difficulties in completeness of coverage in time. A high proportion of cases with unknown primary anatomical site indicate lack of complete work-up of cancer cases and deficiencies associated with the system of death registration and certification. The lack of death registration may be the cause of the reported lower mortality rates in a few registries. On the other hand what ever be the shortcomings in the existing pattern of NRCP, this is at present the best possible data considering the scarcity of resources and motivation. The existing registry data give a satisfactory reflection of the cancer burden in their respective areas. The existing data has also been verified in terms of its completeness of coverage (of cancer cases) and its reliability before declaring it authentic. Considering the fact that cancer registry is essential to formulate any cancer control program at a national level (NRCP 2001), the registries under NRCP in this respect have provided baseline parameters with data of high quality and scientific validity. Systemic summation of data despite from only a few centres has at least suggested some indicators to the pattern and burden of cancer disease amenable to control measures. It has moreover also highlighted the need for undertaking the etiological studies in several sites of cancer. Moreover some other registries are cropping up across the country but their final data are still awaited.

Table 6. Established Cancer Registries of India

Zones	Registries	ASR Male	ASR Female
North	Delhi	123.7	135.6
Central	Bhopal		
West	Ahemedabad	107.2	82.9
East	Kolkatta	102.1	114.6
South-West	Mumbai	116.3	122.4
	Poona	103.9	115.3
	Nagpur	118.4	118.8
South	Madras	108	118
	Trivendram	87.8	81.1
	Banglore	88.3	110.7
	Karunaggappalli*	102.6	76
Rural	Barshi		

*HBCR: hospital based cancer registry

It is important to stress the health care system of the country. Since description for every state is not possible in this article it is worth mentioning the status of Uttar Pradesh, one of the most populated state of the nation (adapted from 'The Times of India' daily Lucknow Edn. 27-JUN-2005) (Mohan A 2005). "Today UP has the largest public sector health infrastructure. Almost for every 6000 population there is some public sector health facility available (at least a subcenter). However only 9% of people actually make use of this in case of ordinary ailments. Unlike the normal perception, a very large number of private sector health providers exist in the state , a vast majority of which are quacks. Surprisingly 48% of population of UP is treated by quacks and another 8% by faith-leaders. Even well off households (43.1%) make use of these quacks. In contrast the government health care providers are infrequently visited. The World Bank report projects that one of the major reason for poverty in UP is the health related expenses and burden of hospitalization. Despite the fact that more than half of the state population is being treated by quacks, various legislations and court orders including drives have been a failure, as these quacks still exist and are preferred. Ironically the state lacks a proper listing of genuine health care providers." With this health system it is not difficult to imagine the fate of a cancer patient particularly a patient with head and neck (H&N) cancer where a thorough clinical examination is essential for early detection. Moreover the existing treatment facilities for cancer control in terms of radiotherapy and financial allocation are woefully inadequate to take care of even the present load (Murthy et al., 2008). Not the least the overall awareness of oral cancer at different places amongst high risk population is grossly inconstant particularly amongst youngsters (Agarwal et al., 2012; Elango et al., 2009). Surprisingly the findings (Kumar and Suresan 2012) concerning qualified dentists' knowledge and opinion related to oral and pharyngeal cancer strongly suggest that educational interventions for practitioners are necessary to enhance cancer detection/prevention. Under these circumstances it is particularly impossible to obtain absolute reliable data pertaining to H&N cancer incidence.

Sankarnarayanan et al. (1998) in a global perspective on epidemiology and prognosis of H&N cancer clearly reported the ASR in Indian males to exceed 30 per 100,000 and in Indian females to exceed 10/100,000. The highest ASR in males is reported from France, but the highest ASR in females is reported from India. They further reported a declining trend in both sexes in India and predicted them to be reflection of underlying trends in the cancer of the major sub sites that seem to be related to the changing prevalence of the risk factors. However on comparing the cancer incidence across the various regions of the countries, it is evident that the south zone of India has a less incidence of cancer as compared to the other areas. Swaminathan et al. (2009) studying rural districts of south India concluded that cancer incidence to be significantly lower, cancer patterns to be markedly different and population based cancer survival to be lower in rural than urban areas thus necessitating the estimation of realistic cancer burden. Manoharan et al. (2010) have reported a statistically significant difference in cancer rates in rural vs. urban Delhi wherein the former the rates are even lower than other rural registries of the country.

Net Based Atlas of Cancer in India

Under the auspices of World Health Organization, a project on 'Development of an Atlas of cancer in India' was commenced in 2001. Information on 217,174 microscopically diagnosed cases (MAAR) by gender and site was calculated. As per this atlas districts emerging as new sites for highest incidence of different cancers world wide are: Aizawl - tongue (10.2) and hypopharynx (16.1); Kolar - mouth (10.7). Five districts (Wardha, Kanyakumari, Pondicherry, Tiruvanthapuram and Kollam) have mouth cancer incidence ranging from 9.1 to 14.1 - much higher than recorded world wide. Since the present population covers only 13% of population and there is still no data available for more than 500 districts in the country , this report should be treated as just a preliminary venture. However few facts stand out rightly since this report has identified hot spot of high incidence, geographic belts with specific cancers and likely zones for setting up population based registries (Nandkumar et al., 2005). Moreover the 'tip of iceberg' hypothesis is further supported by this atlas report. As a consequence of this project, a North-Eastern cancer registry has been commenced in 6 areas at Guwahati, Dibrugarh, and Silchar in Assam, Aizawl in Mizoram, Imphal in Manipur and Gangtok in Sikkim. These registries have started functioning from 01-JAN-2003.

This article reviews the entire head and neck cancer scenario in India. The discussion intends to focus upon the various head and neck cancers as per their respective

Table 7. Head and Neck Cancer incidence (ASR) Across the World

Country	LIP		Tongue		Mouth		Tonsil	
	M	F	M	F	M	F	M	F
USA	4.1 (NM)	0.7 (NM)	Wht=4.2 (NJ) Blk=3.0 (Ct)	1.4 (LA) Blk=1.5 (Ct)	Wht=7.5 (Ct) Wht=1.6 (Dt)	Wht=2.0 (Ct) 0.5 (Dt)	Blk=3.9 (Dt)	0.8 (Dt)
Canada	9.8 (NF)	3.1 (Y)	Blk=2.6 (Qb)	1.0 (O)	4.1 (Y)	3.2 (Y)	1.4 (Y)	0.5 (Mt)
Brazil	2.6 (Cp)	0.8 (Cp)	3.7 (Cp)	0.9 (G)	3.9 (G)	1.4 (G)	0.8 (G)	0.5 (G)
Argentina	2.2 (BB)	0.7 (Cn)	3.8 (Cn)	0.5 (Cn)	4.4 (Cn)	0.7 (BB)	0.9 (Cn)	0.5 (BB)
France	3.9 (Mn)	0.5 (Mn)	7.5 (Cl)	1.6 (D)	9.1 (Cl)	1.6 (Mn)	6.5 (Cl)	0.8 (Sm)
Italy	3.5 (Ss)	0.4 (RP)	4.8 (BP)	1.0 (FP)	5.0 (VC)	1.3 (VC)	1.6 (BP)	0.5 (NE)
U.K.	1.9 (NI)	0.3 (NI)	2.1 (S)	0.9 (S)	3.3 (S)	1.4 (S)	0.9 (NWE)	0.3 (NWE)
China	0.7 (Tw)	0.1 (Tw)	5.1 (Tw)	1.0 (HK)	9.3 (Tw)	1.1 (Tw)	1.2 (Tw)	0.1 (Tw)
India	**0.9 (P)**	**0.4 (Tr)**	**9.3 (Ah)**	**2.7 (Tr)**	**9.3 (Tr)**	**7.5 (Bg)**	**2.8 (Ah)**	**0.5 (Del)**
Japan	0.1 (NP)	0.1 (NP)	2.2 (HP)	1.1 (HP)	2.2 (NP)	0.9 (NP)	0.4 (NP)	0.1 (Np)
Australia	10.9 (QN)	2.6 (Tm)	2.9 (Qn)	1.4 (Qn)	3.6 (NT)	1.4 (CT)	4.4 (NT)	0.6 (NT)
New Zealand	1.6	0.6	1.6	0.6	1.4	0.7	0.7	0.2
Uganda	-	-	0.3	0.1	1.9	1.7	0.7	0.1
Zimbabwe	-	0.3 (H)	0.7	0.6	1.3	0.8	0.1	0.1

*Aabbreviations of the registries: NF (Newfoundland); Cp (Campinas); BB (Bahia Blanca); Mn (Manche); Ss (Sassari); NI (North Ireland); Tw (Taiwan); P (Poona); Qn (Queensland); NM (New Mexico); Y (Yukon); Cn (Concordia); RP (Ragusa province); NI (Northern Ireland); Tr (Trivandrum); Tm (Tasmania); NJ (New Jersey); Qb (Quebec); Cl (Calvados); BP (Biella province); Sc (Scotland); Ah (Ahemdabad); HP (Hiroshima Prefecture); LA (Los Angeles); O (Ontario); G (Goiania); D (Doubs); FP (Ferrara province); HK (Hong kong); Ct (Connecticut); VC (Venetian city); NT (Northern territory); CT (Central territory); Bg (Bangalore); Dt (Detroit); Mt (Manitoba); NWE (North western England); Sm (Somme); NE (North east); Del (Delhi); NWT (North western territory); HR (Haut Rhin); VP (Varese Province); M&CE (Merseyside and Cheshire England); Mad (Madras); YP (Yamagata Prefecture); NSW (New South Wales); RP (Ragusa Province); MP (Miyagi Prefecture); BR (Bas Rhin); SP (Saga Prefecture); LNO (Louisiana New Orleans); VR (Venetian region); Tn (Tianjin); H (Hiroshima); NP (Nagasaki Prefecture); OR (Oxford region); PR (Parma Province); SF (San Francisco); CLA (California: LA); Trn (Tarn); Rm (Romagna); Fr (Ferrara); Hr (Herault)

Table 8. Head and Neck Cancer Incidence (ASR) Across the World

Country	Hypopharynx M		Hypopharynx F		Larynx M		Larynx F		Nose/PNS M		Nose/PNS F	
USA	Blk=3.7	(Ct)	Blk=1.0	(Ct)	Blk=17.3	(LNO)	Blk=2.4	(LNO)	Blk=1.2	(Lcr)	Ind=1.1	(NM)
	Wht=1.2	(Ct)	Wht=0.2	(Ct)	Wht=7.9	(LNO)	Wht=2.0	(LNO)	Wht=0.6	(Lcr)	Wht=0.3	(NM)
Canada	1.4	(Mt)	0.3	(Mt)	8.0	(Qb)	1.6	(Qb)	0.7	(O)	0.6	(NF)
Brazil	2.8	(Cp)	0.5	(Cp)	7.4	(Cp)	1.5	(G)	0.9	(G)	0.4	(Cp)
Argentina	0.6	(Cn)	0.5	(Cn)	10.2	(Cn)	1.6	(Cn)	1.7	(Cn)	0.7	(Cn)
France	12.9	(BR)	0.7	(BR)	13.0	(Sm)	0.8	(Mn)	1.4	(Cl)	0.4	(HR)
Italy	4.1	(NE)	0.6	(BP)	14.1	(VR)	1.3	(BP)	1.4	(BP)	0.8	(BP)
U.K.	1.3	(S)	0.4	(S)	6.3	(S)	1.4	(S)	0.7	(M&CE)	0.4	(NWE)
China	2.8	(Tw)	1.0	(Tw)	5.8	(HK)	1.7	(Tn)	0.8	(HK)	0.4	(HK)
India	**7.6**	**(Ah)**	**1.9**	**(Mad)**	**9.7**	**(Ng)**	**1.4**	**(Del)**	**1.2**	**(Pn)**	**0.6**	**(Pn)**
Japan	1.4	(SP)	0.3	(YP)	4.2	(NP)	0.2	(H)	1.2	(MP)	0.5	(MP)
Australia	4.4	(NT)	0.3	(Tm)	9.8	(NR)	1.2	(NR)	1.2	(Tm)	0.6	(CT)
New Zealand	0.6		0.1		3.2		0.5		0.5		0.3	
Uganda	0.2		0.5		1.3		1.1		1.3		1.0	
Zimbabwe	0.8		1.0		4.9		0.9		1.2		0.8	

*Aabbreviations of the registries: see table 7

Table 9. Head and Neck Cancer Incidence (ASR) Across the World

Country	Nasopharynx M		Nasopharynx F		Salivary gland M		Salivary gland F		Thyroid M		Thyroid F	
USA	Chinese=2.4	(LA)	Blk=1.4	(Ct)	Blk=1.0	(SF)	Filipino=5.0	(CLA)	Filipino=12.1	(CLA)		
	7.6	(LA)										
	White=0.3	(LA)	Wht=0.9	(Ct)	Wht=2.9	(CLA)	Wht=7.6	(CLA)				
	0.5	(LA)										
Canada	9.2	(NWT)	6.0	(NWT)	4.0	(NWT)	3.8	(NWT)	2.6	(O)	6.2	(NF)
Brazil	0.8	(Cp)	0.4	(G)	1.3	(G)	1.2	(G)	2.1	(G)	6.0	(G)
Argentina	0.4	(BB)	0.1	(BB)	0.9	(Cn)	0.9	(Cn)	1.1	(BB)	2.8	(BB)
France	1.2	(HR)	0.3	(D)	1.2	(HR)	0.7	(BR)	2.3	(Hr)	12.0	(Trn)
Italy	1.2	(VP)	0.6	(RP)	1.0	(NE)	0.9	(PP)	3.5	(Fr)	9.4	(Rm)
U.K.	0.6	(MC&E)	0.3	(NWE)	0.7	(OR)	0.6	(OR)	1.4	(NI)	3.4	(NI)
China	21.4	(HK)	8.3	(HK)	0.9	(HK)	0.8	(HK)	1.9	(HK)	7.1	(HK)
India	**0.8**	**(Mad)**	**0.3**	**(Mad)**	**0.6**	**(Ah)**	**0.6**	**(Nag)**	**1.8**	**(Tr)**	**5.1**	**(Tr)**
Japan	0.9	(YP)	0.3	(MP)	0.6	(H)	0.4	(H)	2.2	(NP)	10.5	(H)
Australia	0.9	(NSW)	0.6	(NT)	1.9	(NT)	0.7	(Qn)	2.2	(NSW)	6.4	(NT)
New Zealand	0.8		0.2		0.8		0.4		1.7		3.5	
Uganda	1.8		1.4		0.4		0.8		0.6		4.6	
Zimbabwe	0.5		0.7		0.9		0.7		0.7		3.6	

*Aabbreviations of the registries: see table 7

sub-sites in India and the corresponding situation in the rest of the world as per the population based registries (International Agency for Research on Cancer - World Health Organization: IARC-WHO) primarily (Tables 7-11).

Cancer of Lip

This particular cancer has a low incidence in India (Table 7). The lower lip receives considerable sunlight exposure than the upper lip that is comparatively shaded (even without a moustache) accounting for a higher occurrence than the later. Indian race with a tanning skin and a higher melanin content naturally protects against the ultraviolet induced actinic skin changes, hence the majority of the population (farmers and labourers) working outdoor in the scorching sunlight is less effected. Accordingly no incidence has been reported in the black races from Uganda and Zimbabwe either. Earlier literature suggested tobacco in the form of pipe smoking as a possible etiologic agent (Molnar et al., 1974) where the high temperature generated within the stem from the smoke was implicated as an irritant. The different types of pipes practiced in India such as hooka, chillum are still not uncommon, and can be seen especially in rural areas.

Table 10. Head and Neck Cancer Incidence (ASR) in India

Country	Ahemdabad M	Ahemdabad F	Bangalore M	Bangalore F	Madras M	Madras F	Delhi M	Delhi F
Lip	0.3	0.2	0.2	0.1	0.3	0.2	0.4	0.2
Tongue	9.3	1.9	3.2	0.8	5.6	1.7	6.1	1.8
Mouth	6.5	2.7	2.7	7.5	6.6	5.4	4.4	2.6
Tonsil	2.8	0.3	1.1	0.3	1.3	0.2	2.1	0.5
Nasopharynx	0.3	0.2	0.4	0.3	0.8	0.3	0.5	0.2
Hypopharynx	7.6	1.6	5.5	1.4	5	1.9	2.7	0.4
Larynx	6.1	0.4	3.7	0.5	4.7	0.5	9.4	1.4
Nose/PNS	0.6	0.4	0.5	0.4	0.8	0.5	0.4	0.3
Salivary gland	0.6	0.4	0.4	0.3	0.5	0.3	0.5	0.5
Thyroid	0.3	0.8	0.9	2.7	1.1	1.6	0.9	2.1

Table 11. Head and Neck Cancer Incidence (ASR) in India

Tumour site	Karunagappally M	Karunagappally F	Bombay M	Bombay F	Nagpur M	Nagpur F	Poona M	Poona F	Trivandrum M	Trivandrum F
Lip	0.5	0.2	0.3	0.3	0.5	0.3	0.9	0.3	0.5	0.4
Tongue	4.5	1.7	5.7	2.4	5.9	1.6	3.6	1.7	5.4	2.7
Mouth	6.6	3.5	5.7	4.3	6.1	3.8	7.8	5	9.3	4.7
Tonsil	0.5	0.2	1.7	0.3	2	0.4	1.1	0.4	0.8	0.3
Nasopharynx	0.2	0.1	0.5	0.3	0.2	0.3	0.6	0.1	0.6	0.2
Hypopharynx	2.1	0.3	5.9	1.8	6.1	0.6	3.4	1.2	2.1	0.3
Larynx	3.5	0	7	1.2	9.7	0.9	7.6	1.3	4.2	0.1
Nose/PNS	0.8	0.3	0.8	0.6	0.5	0.6	1.2	0.6	0.4	0.3
Salivary gland	0.3	0.2	0.5	0.3	0.6	0.7	0.6	0.2	0.5	0.4
Thyroid	0.7	4.9	0.8	2	0.6	2	0.8	1.1	1.8	5.1

On the contrary the incidence in females is less and in general does not seem to differ markedly from the rest of the world probably owing to more indoor orientation. Currently in India it is not uncommon to see female being increasingly employed as masons and labourers in the developing cities, but still the majority (70%) of rural population amongst the less poor classes still does not encourage female labour. Southern and south-western parts of the country have more incidence of the cancer lip as compared to the north and west. The use of synthetic facial cosmetics including lipsticks either due to cultural background (heritage dances etc) or secondary to the 'open' exposure by the film industry (Bollywood and Malayalam) may predispose to local irritation. The habit of 'lip to lip' kissing in public is rare (social taboo) in India. This may theoretically decrease the possibility of 'oral-transmission' of oncogenic agents/ viruses etc in India, thereby contributing to the low incidence of cancer lip as compared to other countries. The habit of applying dry lime and 'kaththa' (Acacia ketachu) on the superficial mucosal lesion/ abrasion for healing is a common practice in north central India. The known corrosive effects of this medication further causes irritation and hence predisposition to the cancer. The usual practice of 'pouching tobacco', with or without lime in the gingivo-buccal sulcus (for example 'khaini tobacco' used in north eastern parts of the country mainly Bihar) also effects the mucosal surfaces of the lip by the trickling 'contaminated' saliva to cause cancer predisposition. This also affects the lower lip more commonly than the upper one. About 42% of the users keep it in front (Stich et al., 1982), thus predisposing to development of cancer lower lip as being in close proximity. Poor dental hygiene may play a role in the etiology of the lip cancer as sharp jagged teeth, poorly fitting dentures and chronically infected gingiva may cause persistent irritation of lips. The concept of dental hygiene is less well understood by the majority of Indian population. Major sector of people use indigenous mud, clay, charcoal, tobacco-bearing tooth powder, saw dust etc for teeth cleaning. On the contrary a large section of rural population still prefers to use Neem (Azadirachta indica) stem for teeth cleaning, which is in fact considered a good natural agent for tooth and gum hygiene. It may be possible that it is more of the tobacco chewing and smoking habit that affects the normal dental hygiene rather than the effect of the agents used in teeth cleaning. Chronic alcoholism may also be another factor in the development of carcinoma lip as has been found associated with lip cancer to the tune of 47% (Molnar et al., 1974). There are wide varieties of alcohols available in the country from local country-made illegal spirits to legalized commercial products.

Cancer Tongue

Tongue is although the most common intra-oral site of cancer in most countries, its epidemiology shows a significant geographic distribution (Moore et al., 2000). A comparison world wide reveals its incidence in India to be much higher than the other countries (Table 7). Although a remarkably high incidence in India is appreciated at global level amongst both sexes but there seems to be a remarkable difference in sex incidence not only in India but in general across the world. Sankaranarayan et at (1998) reported a decline in trend for cancer tongue in both sexes in India, brazil, and US whites but a corresponding increasing trends in most other populations particularly in the central and eastern Europe, Scandinavia, Canada, Japan and Australia. The overall trends are a reflection of the underlying trends in cancer of major subsites that seem to be related to the changing prevalence of risk factors. Indians (immigrants) have popularized the habit of betal chewing in the new world as well. Yoganathan (2002) reports the same for New Zealand and Australia, where areca nut preparations are through out available.

Parkin et al. (1997) reported downward trends in male incidence of oral cancer in developing countries. Franceschi et al. (1999) stated that in non-smokers, substantial increases in oral cancer appear to be more closely related to changes in alcohol consumption (Franceschi et al., 2000). The optimistic data of decreasing trends in rates as reported by the foreign authors may not truly reflect the current status of use of chewable tobacco, as reported from the north part of India (Meherotra et al., 2003). Jayant et al. (2011) from Barshi have lately shown a marked decrease in five-year relative survival trend between 1988-1992 and 1993-2000 for cancers of the tongue, hypopharynx, and larynx. The maximum rates of cancer tongue has been demonstrated in the west India (Ahemdabad) as particularly in males followed by the north central parts (Delhi) (Tables 10-11). On the contrary the female preponderance is clearly seen in the southern parts of the country. Pillai et al. (1993) from Regional Cancer Center Trivandrum reported an enormous prevalence of oral and oropharyngeal cancer to the tune of 30% amongst all types of cancers seen in the country. The recently developed atlas of cancer (2005) in India reveals the highest MASR (microscopic age standardized rate) in Aizawl in Mizzoram state (10.2/100,000) (Nandkumar et al., 2005). This is even higher than that in PBCR of Bhopal (10/100,000) which was earlier reported to be highest in India(Nandkumar et al., 2005). Iype et at (2004) from Regional Cancer Center Trivandrum reported 43.6% incidence of tongue cancer amongst all the cases of oral cancer below the age 35 years. Nair et al. (1988) in a review of all the cases at Regional Cancer centre Trivandrum reported a 23.97% prevalence of cancer tongue. A high prevalence of tongue cancer may be linked with its maximum propensity of regional spread amongst the oral sub-sites as reported by Yeole et al. (2011). Mehta et al. (1989) confirmed a strong link between bidi smoking and central papillary atrophy of the tongue in rural Indians.

Amongst tobacco chewers about 58% of the users (Stich et al., 1982), move the tobacco towards left or right side within the oral cavity whereby carcinogens percolate admixed with saliva to cause irritation of the adjoining mucosa and tongue. It may be possible to have more predisposition of lateral boarder of tongue as compared to tip since it is relatively less mobile and with larger surface area, and hence more exposed to the carcinogen mixed saliva. There are innumerable types of chewable tobacco and related products manufactured in the country with the name of pan masala, guttka, pukar, khaini, zarda, mishri, super, snuff, tooth-paste and tooth-powder. The betal quid substitutes are basically a flavoured and sweetened dry mixture of areca nut, catechu and slaked lime with tobacco (Guttka) or without tobacco (pan-masala). Even the latter is known to contain substantial amount of nicotine. New trends of tobacco use have been seen in children and adolescents. Kalyani et al. (2010) have reported cancer in adolescent and young adults to account for 26.6% of all the cancers diagnosed between the ages of 15–44 years. Of them the oral cancer was the most common. The youngsters in India are often offered the smokeless tobacco free of cost that has an addicting potential, to make them dependent on a particular brand. This 'business-promotion' of a tobacco product have been possibly the major factor responsible for the changing trends. Rooban et al. (2010) emphasize for effective interventions to control tobacco use as failure to do so would most probably result in doubling the burden of diseases-both communicable and noncommunicable-among India's teening poor.

Cancer Mouth

Incidence of cancer of buccal mucosa is second only to that of cancer. Nair et al. (188) in a review of oral cancer cases from Regional Cancer Center Trivandrum reported the highest prevalence of cancer of buccal mucosa (49.9%) outnumbering that of tongue (23.97%). It is to be noted that the younger patients who develop this subsite of cancer in absence of smoking or chewing tobacco have the worst outcome (Iype et al., 2004). Cancer of the gingiva (gum, alveolar ridge) on the other hand is most unusual before the age 50 and effects women more than men. However lately Shenoi et al. (2012) from Maharashtra have reported mandibular alveolus region as the most common site in their series. Ironically more than 80% had reported late in advanced stage (Stage III onwards). Chronic irritation is an unlikely causative factor in palate cancers although that area is associated with pre-malignant lesions and mucosal atrophy.

Ferlay et al. (1998) stated that India accounts for a quarter of the world burden of oral cancer. Moore et al. (2000) during a global review of the epidemiology of mouth cancer emphasized the paucity of reliable data from the developing countries but still after comparing, the incidence rates in India far outnumber the rest of the world in both sexes. The 'culture' of using tobacco and related products (specially chewable tobacco) is very common amongst indoor females and it appears that there is no difference from their outdoor counterparts (males); hence the comparable rates. China and France closely follow the Indian rates particularly in males but there is a substantial difference amongst the sexes in those countries. The substantial difference between the incidence amongst blacks from America and that from Africa may further suggest a predominant environmental impact of cancer predisposition in this sub-site. Moreover genetic/ethnic contribution cannot be ignored considering a substantial difference amongst the ASR between black and white from the same registry (Connecticut). Amongst the various registries of India it is evident that the rates are maximum in the southern and southwestern parts of the country. The north India has a low incidence but this may be due to gross under-representation of that part of the country by just a single registry. Noteworthy is that all the centres reflect a male predominance with comparable dissimilarities amongst sexes, except in Bangalore registry where female incidence is substantially higher than the males. An optimistic data depicts the time trends in the decreasing incidence and risk of developing cancer in Indian population based in Mumbai (Sunny et al., 2004). In males a statistically significant decreasing trend in overall ASR were observed during 1986 to 2000, with a yearly decrease of 1.7%. This decrease was significant for men above the age of 40, but for young adult men below 40, there was no significant decrease, the level being stable. In females the overall decreasing trends in ASR of the oral cancers was not significant except for the age group 40-59 yrs where a significant decline was observed. The probability estimates indicated that one out of every 57 men and 95 women will encounter oral cancer somewhere in their lives and 97% of chances exist after crossing the age of 40 years. In a recent study on pattern of cancer in adolescent and young adults by Kalyani et al. (2010), male to female ratio was found to be 1:2 and cancer of mouth was the leading site in both sexes. A national cancer mortality through nationally representative survey (Dikshit et al., 2012) revealed oral (lip and pharynx) cancer to be the most leading cause of death amongst males in the age group of 30-69 years. Byakodi et al. (2012) have lately reported an overall prevalence of oral cancer to the tune of 1.12% amongst all the outpatients attending a dental hospital at Sangli Maharashtra.

The recently developed Atlas of Cancer in India (2005) (Nandkumar et al., 2005) reveals the highest MASR amongst females in Kolar district (10.7 per 100,000) in Karnataka state, followed by Bangalore rural, Kollam district in Kerela and Villupuram district in Tamilnadu state and Pondicherry district (under the Union Territory of Pondicherry). The highest incidence (MSAR) amongst males is reported from Wardha (14) followed by Kanyakumari (Tamil Nadu), Kollam (Kerela), Thiruvanthapuram (Kerela) and Pondicherry as per Atlas of Cancer in India, (2005). Raybaud et al. (2003) after analysing the international literature concluded some genetic alterations in oral Head and Neck squamous cell cancer in India and south-east Asia. They found that activation of RAS and MYC oncogenes appear to be related with the presence of specific carcinogens in snuff and tobacco. A racial (genetic) variation was appreciated in a study where ASR of oral cavity cancers were found to be lower in Parsis than the non-Parsi population (Yeole et al., 2001). Swerdlow et al. (1995) while studying the risk of cancer mortality in persons born in Indian subcontinent who migrated to England and Wales found a significantly high risk in Indian ethnic migrants for cancer of oral cavity and pharynx in both sexes.

Recent reports indicate the involvement of human papilloma virus (HPV) particularly HPV-16 in a subset of squamous cell carcinoma of head and neck cancer. A study on oral cancers in India revealed a number of cutaneous HPVs, predominantly HPV types of genus Beta-papilloma virus (Koppikar et al., 2005). Multiple HPV infections were common in 14% of the series while HPV 16 and 18 were each detected in 6%. However neither high risk HPVs nor multiple infections were observed in the mouth wash samples of control (normal) population. Hence it seems that oral cavity harbours a variety of different HPVs that in conjunction with carcinogens present in tobacco may contribute to cancer development. Kulkarni et al. (2011) from Karnataka published that in oral squamous cell cancer 70.6% were positive for HPV, amongst which HPV-16 prevalence was observed in 45.8%, HPV-18 in 54.2% , and HPV-16 and 18 joint infection in 4.18%. Moreover Jalouli et al. (2012) have warranted further studies to determine the possible role of viral infections and co-infections with HPV, EBV and HSV as risk markers for development of oral squamous cell carcinoma.

The tobacco related products specially ‘Gutka’ and ‘pan-masala’ have been strongly implicated in recent increase in incidence of oral submucous fibrosis, after short period of use specially in very young population. It mainly affects the buccal mucosa and leads to gross hypersensitivity with marked trismus. This pre-malignant condition is extremely debilitating with no known cure. About 2.5 million people are affected by oral submucous fibrosis, mostly in Indian subcontinent (Cox et al., 1996) with an incidence of oral cancer of 7.6% for a median 10 year follow-up period. The smokeless tobacco and betal quid chewing even (with or without tobacco) increases the risk of oral pre-cancers, as reflected by the dose response relationships for both frequency and duration (Jacob et al., 2004).

A study on reverse smoking (ie smoking with the glowing end inside the mouth) revealed that use of tobacco in this form conferred a 5.19 times higher risk of oral precancerous lesions of the palate that did use chewing tobacco (Hebert et al., 20020. The risk of developing hard palate carcinoma for females is 132 times more with reverse smoking of chuttas (Reddy 1974). Reverse smoking allows particulate material (including carcinogens) from the smoke to enter gland openings of the hard palate which do not empty as effectively as do those of soft palate. Thus the exposure is further enhanced with bad oral hygiene due to seldom oral cleansing. The common forms of tobacco smoking in rural India consists of ‘Bidi’ as the commonest followed by chutta (including reverse smoking), ‘hookka’ and clay-pipe.

It has been observed that vitamin deficiencies (A, C, E) may contribute to the high prevalence of the oral cancers in India (Tondon et al., 2000). A study carried out in rural India found that the presence of the lesions was associated in patients with oral pre-cancerous lesions with low plasma levels of vitamin E and beta-carotene (Patel et al., 2001). Most of the oral cancers in India are linked with diet, weight and other lifestyle factors including betal quid (paan) chewing(Tondon et al., 2000). Body mass index (BMI) has been inversely associated with oral cancer, and paan chewers with low BMI has a very high risk of oral cancer (Rajkumar et al., 2003). Sharma et al. (2010) have observed variable incidence of oral cancer within one geographical location as per age, sex, site or habit.

A multifactorial analytical study for the delay in presentation of oral cases was carried out at Lucknow (Kumar et al., 2001) which demonstrated following five variables as significant independent predictors of primary delay: 1. ill-fated to have cancer, 2. cancer a curse, 3. non-availability of transport, 4. trivial ulcers in mouth are self-limiting, 5. prolonged treatment renders family stressful. These cancer related myths can only be overcome by better education. Byakodi et al. (2012) from a big city (Banglore) of India further stressed that education about ill effects of tobacco and alcohol consumption is necessary at a broader scale

Cancer Oropharynx

The cancer of oropharynx is very common in India. The incidence of tonsil cancer in India in males is highest in the west (Ahemdabad) followed closely by the northern parts (Delhi) while in females the maximum ASR is seen in the northern parts of the country. The maximum ASR incidence of cancer tonsil is reported from Somme (France) for males and Vaud (Switzerland) for females (not shown in Table). The incidence of cancer at other sub-sites of oropharynx apart from tonsil shows a similar trend across the globe with France (Calvados) reporting the maximum incidence in males and Australia (Northern territory) revealing maximum rates in females. Amongst the national registries, Trivandrum (South) shows the highest incidence for cancer of other oropharyngeal sub-sites excluding tonsil for males (Table 10 and 11). It is worth noting that although Ahemdabad showed maximum incidence in comparison to Trivandrum for cancer of tonsil in males; but the situation is just the reverse when malignancies of the other sub-sites of the oropharynx are considered. The low incidence in north India may again be due to under-representation of the actual population through a single cancer registry. The recently developed Atlas of Cancer in India (2005) (Nandkumar et al., 2005) clearly reports the higher prevalence along the west coast. Although no registry is based in Rajasthan but a report of cancer profile in western Rajasthan (Sharma and Maheshwari 1992) showed the highest incidence of oropharyngeal and hypopharyngeal malignancies in males with a sex ratio of 1.28:1. It is noteworthy that this was the region where India’s first nuclear explosion took place in 1974.

Tobacco smoking, ionizing radiations, dental carries and poor oral hygiene have all been linked to oropharyngeal cancers. The association with alcohol consumption is well known (Kissin et al., 1973). It appears to act synergistically with tobacco leading to a disproportionate increase in cancer (Schottenfield, 1979). Recently there has been a great interest in the role of human pappillomavirus as a carcinogenic agent. Since this is a well recognized causative factor for uterine cervical cancer, its oropharyngeal implication can possibly be due to its transmission by lip to lip kissing or through oral sex (Mishra and Verma, 2012). The molecular pathway used by HPV to trigger malignant transformation is different from that of other well known risk factors (tobacco, alcohol) associated with squamous cell cancer and since it has a prognostic significance, the HPV infection should be determined in all oropharyngeal cancers (Bisht et al., 2011). In 1984 Bhopal Gas Tragedy, the local population exposed to high levels of methyl isocynate showed a marginally increased risk for cancer of oropharynx (Dikshik and Kanhare 1999) suggesting it to be a potential risk factor.

Cancer Nasopharynx

Nasopharyngeal carcinoma (NPC) in India has a low incidence and is comparable to the world except in some ethnic groups in north eastern (NE) regions particularly Nagaland, Manipur and Mizoram. It seems that there are some significant ethnic and geographical variables within the country predisposing the population of NE India for high incidence of nasopharyngeal carcinoma. The genetic predisposition is reflected by a 10 folds high ASR in the Chinese race in USA compared to the whites. The environmental contribution on the other hand is reflected by a significant decrease in ASR of Chinese race in USA to 30% compared to the native China. Considering the 1981 census figure for population structure of Nagaland (a representative area of NE India), the incidence of nasopharyngeal carcinoma was approximately 6.2 and 2.1 per 100,000 population amongst males and females respectively (Kumar et al., 1996). The striking feature of NPC in NE India is that the incidence ranges from the lowest (as 0.5/100,000 to 2.0/100,000 among Caucasoids) to the highest (as 20/100,000 among Cantonese/Zhongshan dilect Chinese) (Kataki et al., 2011). Another study has revealed that these Naga tribes representing mongoloid groups are more vulnerable to this disease (Zinyu et al., 1990). Thus it can be inferred that nasopharyngeal carcinoma is relatively higher among the mongoloid group of people in NE India as compared to the other Caucasian population of India. The incidence is low in south India with Madras still showing the highest incidence in both sexes amongst all the population based registries across the country. The north parts of the country being in the close approximation with China and sheltering the majority of mongoloid race reveal a lower incidence of nasopharyngeal cancer. This ‘disparity’ may again be due to non-representation of the upper north and NE region. The drainage area of Nepal, Bhutan, and other hilly areas is more in Uttar Pradesh, Uttaranchal and Bihar and then to Chandigarh, Simla and Delhi, and hence, unfortunately, the only registry in Delhi may not truly reflect the incidence of nasopharyngeal cancer. Hence it is theoretically possible to have a much higher incidence in north India as compared to south. The recently developed Atlas of Cancer in India (2005) astonishingly reveals the highest MASR in north-east states specially in Kohima district (19.4 per 100,000) in Nagaland state comparable to high rates found in southern Chinese populations (eg Hong Kong=21.4 per 100,000) (Nandkumar et al., 2005). Imphal West, a district in Manipur state also recorded a MASR of 7.4 per 100,000 while several other districts in the states of Mizoram and Manipur recorded high MASR in both sexes (Nandkumar et al., 2005). A high relative frequency has been reported by a previous study from this region (Kumar and Mahanta 1998), as well as appearing in data from the hospital based cancer registry in Dibrugarh Assam (NRCP 2001, 2002). The association of nasopharyngeal carcinoma with Epstein Barr viral infection (EBV) and its genetic susceptibility is well established. It may be possible that environmental factors modulate the viral infections in a genetically predisposed individual resulting into a cancer of nasopharynx by a synergistic effect of all the factors. Other factors as seen in NE states and other geographical areas, and suggested to be causative are chronic rhino-sinusitis, poor ventilation, inhalation of smoke, and ingestion of salted fish containing dimethylnitrosamine (Armstrong et al., 1983), smoked meat, use of herbal nasal medicine (Chelleng et al., 2000), and preserved foodstuff (Yu 1991). Studies carried out on soot collected from different villages of Nagaland revealed its clastogenic and mutagenic potential (Kumar et al., 1996), thereby suggesting the role of continuous inhalation of such smoke. Clifford (1970) in an analysis of soot showed it to contain significant quantities of benzopyrene, benzanthracene, poly-nuclear aromatic hydrocarbons. Clifford and Bulbrook (1967) reported that smoke particularly from wood, containing carcinogen might get deposited on the posterior and lateral nasopharyngeal walls for several hours in a day for years together. On the other hand Chelleng et al. (2000) in a case-control study in NE region of India did not find any significant association between exposures to smoky atmospheres and nasopharyngeal carcinoma. Hu and Huang (1972) reported a positive association with the use of fossil fuels for cooking and nasopharyngeal carcinoma. Formaldehyde vapour related occupation such as printing industry has revealed an association with nasopharyngeal cancer (Rous et al., 1987). Occupational exposure to products of combustion and cotton dust also have been reported as independent risk factors for nasopharyngeal cancer.

Rathaur et al. (1999) in a pathological study of EBV in nasopharyngeal carcinoma in Indian populations reported the incidence of EBV type A in 74% cases, type B in 25% while co-infection in 3%. Cases from western India showed EBV type A in 57.6% while type B in 7.6%. In contrast patients from eastern India revealed 10% positivity for type B. Although the number of patients were few, the preliminary geographical trends could be obtained. Type-A EBV was hence far more prevalent in western India while in eastern India particularly Assam, all the cases were positive for type-B EBV. Thus a significant variation in the type of EBV infection was observed in nasopharyngeal carcinoma in different ethnic populations in India. Hildesheim et al. (1992) studied the correlation of herbal medicine use and EBV in nasopharyngeal cancer and suggested that herbal medicines have a direct proliferative effect on EBV-transformed cell and thus there is a stronger association of EBV with the development of nasopharyngeal cancer.

Cancer Hypopharynx (and cervical esophagus)

Despite a high incidence of hypo-pharyngeal cancer in India, France still shows a higher incidence (Table 8). The national estimates show the prevalence being comparatively higher in western and southern parts of the country in both sexes (Table 9 and 10). On the contrary the Atlas of Cancer in India (2005) reveals predominance in the N-E regions of the country. The dietary factors might contribute to high risk of hypopharyngeal cancer in India (Heck et al., 2008). In addition to tobacco and alcohol, dietary deficiency particularly vitamin A and iron are implicated in the etiology. The latter deficiency contributes to the post-cricoid pre-malignant condition in females (Plummer-Vinson syndrome). Phukan et al. (2001) have implicated the daily use of Kalakhar for increasing the risk of esophageal cancer. Kalakhar is a highly alkaline material obtained from charred false stem or from the outer layer of a special variety of banana that is used in the preparation of curry or commonly called as 'dal'. They further specified the use of spicy foods and chillies as potential factors increasing the risk for development of cancer esophagus. Nayar et al. (2000) on the other hand quoted several factors such as alcohol, betal leaf chewing with tobacco, bidi smoking and a low vegetable diet as a strong risk factors for esophageal cancer.

Noteworthy the cancer of esophagus is reported (Dhar et al., 1993) to be the most frequent type of cancer in Kashmir valley, which is strikingly different from the rest of India where oral/oropharyngeal cancer is the most common form. This is attributable to the local practice of drinking boiling hot salt tea, along with commonly used fresh and sun-dried vegetables, and red-chillies (Siddiqi et al., 1992). Salted tea made by adding sodium bicarbonate has been shown to have high methylation activity and can result in endogenous formation of nitrosamines (Malkan and Mohandas 1997). Fresh and sun-dried vegetables including chillies too have a high nitrate and nitrosamine content. Khuroo et al. (1992) further reported that incidence rates for esophageal cancer in Muslims, Hindus and Sikhs was different. On the other hand Yeole et al. (2001) reported ASR of cancer of pharynx-esophagus in parsi population to be lower than non-Parsis. Swerdlow et al. (1995) while studying the risk of cancer mortality in persons born in Indian subcontinent who migrated to England and Wales found a significantly high risk in Indian ethnic migrants for cancer of pharynx in both sexes and that of esophagus in females.

Cancer Larynx

Cancer of larynx is fourteenth most common cancer in the world (Tondon et al., 2000). An increased risk has been reported in wood workers exposed to wood dust (Wynder et al., 1956) and in workers of a nitrogen mustard factories (Kurozumi et al., 1977). A relationship with asbestosis was noted (Morgan and Shettigara 1976) but the risk was only confined to those who smoked. Hiranandani (1975) considered the slaked lime present in the Indian tea mixture as causing irritation leading to leukoplakia and post-cricoid carcinoma. Stocks (1970) correlated tea drinking with laryngeal cancer in females. De Stefani et al. (1987) noted an increased risk in those with infrequent consumption of fruits and vegetables. Kapil et al. (2003) 72 reported a strong association of cancer larynx with vitamin A, vitamin C, and zinc, but they could not comment upon the cause effect relationship. Cigarette smoking is a well known and recognized predisposing factor for laryngeal cancer but in the absence of tobacco use, the alcohol as such was not found to increase the risk for laryngeal malignancy that otherwise would synergistically enhance the risk for cancer (Lowry, 1975). Wynder et al. (1956) hypothesized the differences in tobacco and alcohol consumption to be the underlying cause of the differences in the cancer incidence encountered amongst various socioeconomic, educational, cultural and religious groups. It has been shown that ASR of cancer larynx is lower in parsi population as compared to non-parsis (Yeole et al., 2001). Significant risk for cancer of larynx in males was found in Indian ethnic migrants in England and Wales (Swerdlow et al., 1995).

A comparison amongst different registries across the country reveals the highest incidence amongst males in Nagpur closely followed by Delhi, while amongst females in Delhi closely followed by Poona. Although the Kolkata registry reports ASR of 6.4 in males, but Banerjee et al. (1994) in 10 year retrospective study at a rural area of West Bengal named Bankura reported the laryngeal malignancy to be the commonest cancer encountered in males. A study from Ludhiyana (Malhotra et al., 2001) on a retrospective review of 56,565 histopathological biopsies concluded the malignancy of hypopharynx-larynx as the most common amongst males. Similarly Kapoor et al. (1993) reported from Jammu about cancer larynx as the most common head and neck cancer encountered in that region.

Cancer Nose and Paranasal Sinus

A comparable incidence across the globe is seen for this particular subtype. The main reason can be attributed to the natural history of disease, characterized by late detection in advanced stages. Also the national comparison reveals a low incidence of this malignancy in the north central part of the country that probably should be considered with caution owing to a single registry in existence. The incidence of cancer at this site in India does not show any remarkable difference from other parts of the world (Table 8) both in males and females. Similarly a national comparison shows highest incidence in Madras, but the registries reveal more or less similar incidence in both males and females. An epidemiological study way back in 1968 linked the development of adenocarcinoma to wood workers in furniture industry (Acheson et al., 1968), specially amongst those exposed to wood dust such as mechanist and cabinet workers, while sparing the carpenters and polishers with a minimal exposure to wood dust as such. On the other hand Barton (1977) reported 28 folds increased risk for developing squamous carcinoma of ethmoid sinus amongst those working in nickel industry than normal population. Other occupation prone increased risk is seen in boot makers, makers of mustard gas and isopropanolol, and those using radium paints on watch dials owing to ionizing radiation exposure. Much work needs to be done before establishing definite conclusion.

Cancer Salivary Glands

A global comparison reveals a low incidence in India while an increased incidence of salivary gland carcinoma has been reported amongst Eskimos (Merrick et al., 1986). The national figures reflect more or less comparable incidence rates across the various registries. This unusual similarity can be due to more or less similar (indolent) behaviour of such tumours in terms of clinical presentation, treatment response and prognosis with less of the environmental or genetic aggression to the prevalence of this particular cancer. Although EBV has been consistently associated with lymphoepithelial carcinoma of the salivary glands in the Asian population, there is no evidence of its causal role in other primary salivary gland neoplasm (Tsai et al., 1996). The factors reported to be associated with cancer of salivary glands are prior childhood radiation of head and neck (Katz and Preston-Martin 1984), wood dust (Klitenberg et al., 1984), silica (Zheng et al., 1996), nitrosamines in rubber workers (Straif et al., 1999) and smoking (implicated in case of Warthin's tumour (Pinkston and Cole 1996)). Dietary analysis revealed a possible protective effect for a diet high in polyunsaturated fatty acids (Actis and Eynard 2000). Women with increased risk for salivary gland cancer have shown to reveal a history of early menarche and nulliparity, possibly depicting a hormonal effect (Horn-Ross et al., 1999). Minor salivary gland tumors of sinunasal area and oral cavity have acceptable survival despite high recurrence (Pantvaidya et al., 2012; Vaidya et al., 2012), hence are less likely to be missed.

Cancer Thyroid

Thyroid cancer is more prevalent in Europe and Americas, and is certainly not as common as other cancer types in India. A universal preponderance amongst females is well established world wide. The racial variations are well evident while comparing the ASR amongst Filipino (5.0) and whites (2.9) from a single cancer registry (California) in United States (Table 8). Thyroid cancers in India are reported to have the maximum ASR in Trivandrum amongst both sexes closely followed by Karunagapally amongst females only. The ASR from west (Ahemedabad) is reported to show lower ASR. Natural background radiation has been observed in Karunagapally taluka of Quilon district in Kerela, due to its known reserve of monazite deposits, which emit gamma radiation (Rao, 1999). Even in Thiruvathapuram, a 100 Km away from Karunagapally taluka, the incidence of thyroid cancer in both sexes show higher rates than other areas in the country. However Tomatis et al. (1990) stated equivocal association between risk for cancer and geographic variation in natural background radiation. However therapeutic radiation, radiation fall out from nuclear weapons testing and radiations from nuclear accidents have been observed as high risk factors (Ron et al., 1995). Iodine deficiency leading to goiter predispose to follicular type of thyroid cancer (Agarwal and Mishra, 1997). On the other hand iodine rich areas and iodine supplementation has been shown to increase papillary type of thyroid cancer (Rao 1999). The costal areas of Kerela have a wide availability due to consumption of sea food rich in iodine (Paulose 1990) that may be linked to predominance of papillary cancer and conversely the increase of follicular cancer in regions remote from costal areas. In this context it is worth mentioning that the sub-Himalayan region of the country is iodide- deficient, which is known to have a wide spectrum of thyroid disease. Unfortunately adequate cancer data (population based) is grossly lacking for this area and hence firm conclusions cannot be drawn. However in this part of north-central India, the highest incidence of goiter and also carcinoma of thyroid has been found in Tarai region (Varma 1999). The area of Tarai extending from Gorakhpur in east through Basti, Gonda, Baharaich, Lakhimpur Kheri, Sitapur, Pilibhit, Bariely, Moradabad and Nainital district in north west is endemic. In non-endemic areas like Agra, Etawah, slightly higher incidence of papillary carcinoma is reported over follicular carcinoma and reverse is true in endemic areas (Sarda and Kapur 1990). The demographics in this area (Varma 1999) consisted of 58% population in younger age group below 45 years and overall slight predominance of female (55%). Among 6-14 year olds, goiter caused by iodine deficiency, and that related to thyroid cancer has a prevalence rate of 0.33% to 2.4 % respectively (Chakravarty and Ghosh 2000).

Amongst the sub-group analysis in Mumbai, Parsis revealed a higher rate for thyroid cancer in both sexes as compared to other communities except that their rate in females was lower than the females of Christian community. In a study of occurrence of multiple primary cancers (Engeland et al., 1997), the results indicated that among the smoking associated cancers, the risk of getting thyroid cancer was about 3 fold in males and about 8 fold in females. For thyroid cancer patients the risk of smoking associated cancer as second cancer was 1.7 times higher for males only. This synergy may have a greater importance for Indian population.

Acknowledgements

The author (AM) has been supported by a UICC American Cancer Society International Fellowship for Beginning Investigators. The author would like to further acknowledge Dr Bharat Bhushan Aggarwal PhD, Professor, Department of Experimental Therapeutics, and Dr Ehab Hanna MD, Professor, Department of Head and Neck Surgery, UT MD Anderson Cancer Center, Houston for their expert guidance and extreme encouragement to come up with this review. Moreover Dr Miraj Ahmed, Junior Resident of Department of Otolaryngology KGMU is to be acknowledged for his typing assistance.

References

Acheson ED, Cowdell RH, Hadfield E, Macbeth RG (1968). Nasal cancers in wood workers in furniture industry. *Br Med J*, **2**, 587.

Actis AB, Eynard AR (2000). Influence of environmental and nutritional factors on salivary gland tumorigenesis with a special reference to dietary lipids. *Eur J Clin Nutr*, **54**, 805-10.

Agarwal A, Mishra SK (1997). Iodine deficiency and thyroid cancer. In: a monograph on thyroid cancer, Eds. Saroj K Mishra. *JICA*, 7-10.

Agrawal M, Pandey S, Jain S, et al. (2012). Oral cancer awareness of the general public in Gorakhpur City, India. *Asian Pac J Cancer Prev*, **13**, 5195-9.

Armstrong RW, Armstrong MJ, Yu MC, et al. (1983). Salted fish and inhalants as risk factors for nasopharyngeal carcinoma in Malaysian Chinese. *Cancer Res*, **43**, 2967.

Atlas of Cancer in India (2005). HTTP:www.canceratlasindia.org/chapter6_Report.asp?SiteName=Mout&ReportType=Dist_.

Banerjee AK, Bhattacharya N, Chaudhary MK, et al. (1994). Incidence of malignancy in Bankura (a retrospective study). *J Indian Med Assoc*, **92**, 400-2.

Barton RT (1977). Nickle carcinogenesis of the respiratory tract. *J Otolaryngol*, **6**, 412.

Bisht M, Bisht SS (2011). Human papilloma virus: a new risk factor in a subset of head and neck cancers. *J Cancer Res Ther*, **7**, 251-5.

BSAA (2004). Bureau of South Asian Affairs, Background: India, US department of state Nov 2004.

Byakodi R, Byakodi S, Hiremath S, et al. (2012). Oral cancer in India: an epidemiologic and clinical review. *J Community Health*, **37**, 316-9.

Chakravarty I, Ghosh K (2000). Micronutrient malnutrition present status and future remedies. *J Indian Med Assoc*, **98**, 539-42.

Chelleng PK, Narain K, Das HK, et al. (2000). Risk factors for nasopharyngeal carcinoma: a case control study form Nagaland India. *Natl Med J India*, **13**, 6-8.

Clifford P (1970). A review on the epidemiology of nasopharyngeal carcinoma. *Int J Cancer*, **5**, 287.

Clifford P, Bulbrook RD (1967). Environmental studies in African males in nasopharyngeal carcinoma. *Lancet*, **1**, 1228.

Cox SC, Walker DM (1996). Oral submucous fibrosis. *Aust Dent J*, **41**, 294-9.

De Stefani E, Correa P, Oreggia F, et al. (1987). Risk factors for laryngeal cancer. *Cancer*, **60**, 3087,

Dhar GM, Shah GN, Naheed B, et al. (1993). Epidemiological trend in the distribution of cancer in Kashmir valley. *J Epidemiol Community Health*, **47**, 290-2.

Dikshit R, Gupta PC, Ramasundarahettige C, et al. (2012). Million death study collaborators. Cancer mortality in India: a nationally representative survey. *Lancet*, **379**, 1807-16.

Dikshit RP, Kanhare S (1999). Cancer patterns of lung, oropharynx and oral cavity cancer in relation to gas exposure at Bhopal. *Cancer Causes and Control*, **10**, 627-36.

Elango JK, Sundaram KR, Gangadharan P, et al. (2009). Factors affecting oral cancer awareness in a high-risk population in India. *Asian Pac J Cancer Prev*, **10**, 627-30.

Engeland A, Bjorge T, Haldorsen T, et al. (1997). Use of multiple primary cancers to indicate association between smoking and cancer incidence: an incidence of 500,000 cancer cases diagnosed in Norway during 1953-93. *Int J Cancer,* **70**, 401-7.

Ferlay J, Parkin DM, Pisani P (1998). GLOBOCAN Cancer incidence and mortality world wide. IARC Cancer base 3 (on CD ROM). Lyon: IARC.

Franceschi S, Bidoli E, Herrero R, et al. (2000). Comparison of cancers of the oral cavity and pharynx world wide: etiological clues. *Oral Oncol*, **36**, 106-15.

Franceschi S, Levi F, La Vecchia C, et al. (1999). Comparison of the effect of smoking and alcohol drinking between oral and pharyngeal cancer. *Int J Cancer*, **83**, 1-4.

Hebert JR, Gupta PC, Bhonsle RB, et al. (2002). Dietary exposures and oral precancerous lesions in Srikakulam district, Andhra Pradesh India. *Public Health Nutr*, **5**, 303-12.

Heck JE, Sapkota A, Vendhan G, et al. (2008). Dietary risk factors for hypopharyngeal cancer in India. *Cancer Causes Control*, **19**, 1329-37.

Hildesheim A, West S, De Veyra E, et al. (1992). Herbal medicine use , Epstein Barr virus, and risk of nasopharyngeal carcinoma. *Cancer Res*, **52**, 3048.

Hiranandani LH (1975). Panel on epidemiology and etiology of laryngeal carcinoma. *Laryngoscope*, **85**, 1197.

Horn-Ross PL, Morrow M, Ljung BM (1999). Menstrual and reproductive factors for salivary gland cancer risk in women. *Epidemiology*, **10**, 528-30.

Hu MS, Huang HL (1972). Retrospective study on etiological factors of nasopharyngeal carcinoma. *New Med (Canton)*, **12**, 10.

ICMR (2001). National Cancer Registry Programme, consolidated report of the population based cancer registries incidence and distribution of cancer 1990-96, Bangalore NRCP 2001.

Iype EM, Pandey M, Mathew A et al. (2004). Squamous cell cancer of the buccal mucosa in young adults. *Br J Oral Maxillofac Surg*, **42**, 185-9.

Jacob BJ, Straif K, Thomas G, et al. (2004). Betal quid without tobacco as a risk factor for oral precancers. *Oral Oncol*, **40**, 697-704.

Jalouli J, Jalouli MM, Sapkota D, et al. (2012). Human papilloma virus, herpes simplex virus and epstein barr virus inoral squamous cell carcinoma from eight different countries. *Anticancer Res*, **32**, 571-80.

Jayant K, Nene BM, Dinshaw KA, et al. (2011). Cancer survival in Barshi, India, 1993-2000. *IARC Sci Publ*, **162**, 101-6.

Kalyani R, Das S, Kumar MLH (2010). Pattern of cancer in adolescent and young adults - a ten year study in India. *Asian Pac J Cancer Prev*, **11**, 655-9

Kapil U, Singh P, Bahadur S, et al. (2003). Association of vitamin A, vitamin C and zinc with laryngeal cancer. *Indian J Cancer*, **40**, 67-70.

Kapoor R, Goswami KC, Kapoor B, et al. (1993). Pattern of cancer in Jammu region (Hospital based study 1978-87). *Indian J Cancer*, **30**, 67-71.

Katz AD, Preston-Martin S (1984). Salivary gland tumours and previous radiotherapy to head and neck: report of a clinical series. *Am J Surg*, **147**, 345.

Khuroo MS, Zargar SA, Mahajan R, et al. (1992). High Incidence of esophageal and gastric cancers in Kashmir in a population of special personal and dietary habits. *Gut*, **33**, 11-5.

Kissin B, Kaley MM, Su WH, et al. (1973). Head and neck cancer in alcoholics. The relationship to drinking, smoking and dietary patterns. *JAMA*, **224**, 1174.

Klitenberg C, Olofson J, Hellquist H, et al. (1984). Adenocarcinoma of ethmoid sinuses: a review of 28 cases with special reference to wood dust exposure. *Cancer*, **54**, 482.

Koppikar P, deVilliers EM, Mulherkar R (2005). Identification of human papilloma viruses in tumours of the oral cavity in an Indian community. *Int J Cancer*, **113**, 946-50.

Kotaki AC, Simons MJ, Das AK, et al. (2011). Nasopharyngeal carcinoma in the Northeastern states of India. *Chinese J Cancer*, **30**, 106-13.

Kulkarni SS, Kulkarni SS, Vastrad PP, et al. (2011). Prevalence and distribution of high risk human papillomavirus (HPV) types 16 and 18 in carcinoma of cervix, saliva of patients with oral squamous cell carcinoma and in the general population in Karnataka, India. *Asian Pac J Cancer Prev*, **12**, 645-8.

Kumar S, Heller RF, Pandey U, et al. (2001). Delay in presentation of oral cancer: a multifactorial analytical study.

Natl Med J India, **14**, 13-7.
Kumar S, Mahanta J (1998). Aetiology of nasopharyngeal carcinoma. A review. *Indian J Cancer*, **35**, 47-56.
Kumar S, Zinyu R, Singh IKK, et al. (1996). Studies on nasopharyngeal carcinoma with reference to the north eastern region of India. *Ann Natl Acad Med Sci,* **32**, 199.
Kumar V KV, Suresan V (2012). Knowledge, attitude and screening practices of general dentists concerning oral cancer in Bangalore city. *Indian J Cancer*, **49**, 33-8.
Kurozumi S, Harada Y, Sugimoto Y, et al. (1977). Airway malignancy in poisonous gas workers. *Laryngol Otol*, **91**, 217.
Lowry WS (1975). Alcoholism in cancer of head and neck. *Laryngoscope,* **85**, 1275.
Malhotra V, Shah BS, Sabharwal S (2001). Pattern of cancer in Dayanand Medical College and Hospital, Ludhiyana (a ten year retrospective study). *Indian J Pathol Microbiol*, **44**, 27-30.
Malkan G, Mohandas KM (1997). Epidemiology of digestive cancers in India. I. General principles and esophageal cancer. *Indian J Gastroenterol*, **16**, 98-102.
Manoharan N, Tyagi BB, Raina V (2010). Cancer incidence in rural Delhi. *Asia Pac J Cancer Prev*, **11**, 73-8.
Mehrotra R, Singh M, Kumar D, et al. (2003). Age specific incidence rate and pathological spectrum of oral cancer in Allahabad. *Indian J Med Sciences*, **57**, 400-4.
Mehta FS, Bhonsle RB, Murti PR, et al. (1989). Central papillary atrophy of the tongue among bidi smokers in India: a 10 years study of 182 lesions. *J Oral Pathol Med*, **18**, 475-80.
Merrick Y, Albeck H, Nielsen NH, et al. (1986). Familial clustering of salivary gland carcinoma in Greenland. *Cancer,* **57**, 2097
Mishra A, Verma V (2012). Oral Sex and HPV: population based indications. *Indian J Otolaryngol Head Neck Surg,* 1-7.
Mohan A (2005). UP's Health system riddled with quacks (State of UP's economy). The Times of India daily Lucknow edition 27th June 2005, page 4.
Molnar L, Ronay P, Tapolcsanyi L (1974). Carcinoma of the lip: analysis of the materials of 25 years. *Oncology*, **29**, 101.
Moore SR, Johnson NW, Pierce AM, et al. (2000). The epidemiology of mouth cancer: a review of global incidence. *Oral Dis*, **6**, 65-74.
Morgan RW, Shettigara PT (1976). Occupational asbestos exposure, smoking and laryngeal carcinoma. *Ann NY Acad Sci,* **271**, 308-10.
Murthy NS, Chaudhry K, Rath GK (2008). Burden of cancer and projections for 2016, Indian scenario: Gaps in the availability of radiotherapy treatment facilities. *Asian Pac J Cancer Prev*, **9**, 671-7.
Murthy NS, Juneja A, Sehgal A, et al. (1990). Cancer projection by the turn of century - Indian scene. *Ind J cancer*, **27**, 74-82.
Nair MK, Sankarnarayanan R, Padmanabhan TK (1988). Clinical profile of 2007 oral cancers in Kerela, India. *Ann Dent*, **47**, 23-6.
Nandakumar A, Gupta PK, Gangadharan P, et al. (2005). Epidemiology, Geographic pathology revisited: development of an atlas of cancer in India. *Int J Cancer*, **116**, 740-54.
Nayar D, Kapil U, Joshi YK, et al. (2000). Nutritional risk factors in esophageal cancers. *J Assoc Physicians India*, **48**, 781-7.
NCCP (2006). National cancer control program.
NRCP (2002). National Cancer registry Programme (NRCP-ICMR). Ten year consolidated report of the hospital based cancer registries 1994-98, Bangalore, 2002.
NRCP (2001). National Cancer registry Programme (NRCP-ICMR). Ten year consolidated report of the hospital based cancer registries 1984-93, Bangalore: NRCP 2001.
Pantvaidya GH, Vaidya AD, Metgudmath R, et al. (2012). Minor salivary gland tumors of the sinonasal region: results of a retrospective analysis with review of literature. *Head Neck*, **34**, 1704-10.
Parkin DM, Whelan SL, Ferlay J, et al. (1997). Cancer incidence in five continents volume VII (IARC Scientific Publication no. 143) Lyon : IARC 1997.
Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB (eds) (1997). Cancer Incidence in Five Continents (vol VIII). IARC, Scientific Publication no. 155, Lyon 1997 (ISBN 92 832 21 55 9).
Patel PS, Raval GN, Patel DD, et al. (2001). A study of various sociodemographic factors and plasma vitamin levels in oral and pharyngeal cancer in Gujarat, India. *Asian Pac J Cancer Prev*, **2**, 215-24.
Paulose KP (2011). Hypothyroidism in Kerela (editorial). *Kerela Med J*, **11**, 139-40.
Phukan RK, Chetia CK, Ali MS, et al. (2001). Role of dietary habits in the development of esophageal cancer in Assam, the north eastern region of India. *Nutr Cancer*, **39**, 204-9.
Pillai MR, Nair MK, Kannan S, et al. (1993). Immunopathological and immunological features of oral precancers. *Singapore Dent J*, **18**, 28-38.
Pinkston JA, Cole P (1996). Cigarette smoking and Warthin's tumour. *Am J Epidemiol*, **114**, 183-7.
Rajkumar T, Sridhar H, Balaram P, et al. (2003). Oral cancer in Southern India: the influence of body size, diet infections and sexual practices. *Eur J Cancer Prev*, **12**, 135-43.
Rao DN (1999). Epidemiological observations. In Shah D, Samuel AM, Rao RS (Eds) thyroid cancer: an Indian perspective. *Mumbai, Quest Publications*, 3-16.
Rathaur RG, Chitale AR, Banerjee K (1999). Epstein Barr virus in nasopharyngeal carcinoma in Indian patients. *Indian J Cancer*, **36**, 80-90.
Raybaud H, Odin G, Fafet A, et al. (2003). Genetic alterations in oral and head and neck squamous cell carcinoma: analysis of international literature. *Pathol Biol*, **51**, 176-84.
Reddy CR (1974). Carcinoma of hard palate in India in relation to reverse smoking of 'chuttas'. *J Natl Cancer Inst*, **53**, 615-9.
Ron E, Lubin JH, Shore RE, et al. (1995). Thyroid cancer after exposure to external radiation - A pooled analysis of seven studies. *Radiat Res*, **141**, 259-77.
Rooban T, Elizabeth J, Umadevi KR et al. (2010). Sociodemographic correlates of male chewable smokeless tobacco users in India: a preliminary report of analysis of National Family Health Survey, 2005-2006. *Indian J Cancer*, **1**, 91-100.
Rous GC, Walrath J, Stayner LT, et al. (1987). Nasopharngeal cancer, sinunasal cancer and occupation related to formaldehyde: a case control study. *J Natl Cancer Inst*, **76**, 1221.
Sankaranarayanan R, Masuyer E, Swaminathan R, et al. (1998). Head and neck cancer: a global perspective on epidemiology and prognosis. *Anticancer Res*, **18**, 4779-86.
Sarda AK, Kapur MM (1990). Thyroid Cancer. A report of 206 cases from an area with endemic goiter. *Acta Oncol*, **29**, 863-7.
Schottenfield D (1979). Alcohol as a co-factor in the etiology of cancer. *Cancer*, **43**, 1962.
Sharma P, Saxena S, Aggarwal P (2010). Trends in the epidemiology of oral squamous cell carcinoma in western UP: An institutional study. *Indian J Dent Res*, **21**, 316-9.
Sharma RG, Maheshwari MS, Lodha SC (1992). Cancer profile in western Rajasthan. *Indian J cancer*, **29**, 126-35.
Shenoi R, Devrukhkar V, Chaudhuri, et al. (2012). Demographic and clinical profile of oral squamous cell carcinoma patients: a retrospective study. *Indian J Cancer*, **49**, 21-6.
Siddiqi M, Kumar R, Fazili Z, et al. (1992). Increased exposure

to dietary amines and nitrate in a population at a high risk of esophageal and gastric cancers in Kashmir (India). *Carcinogenesis*, **13**, 1331-5.
Stich HF, Curtis JR, Parida BB (1982). Application of the micronucleus test to exfoliated cells of high cancer risk groups: tobacco chewers. *Int J Cancer*, **30**, 553-9.
Stocks P (1970). Cancer mortality in relation to national consumption of cigarettes, solid fuel, tea and coffee. *Br J Cancer*, **24**, 215.
Straif K, Weiland SK, Bungers M et al. (1999). Exposure to nitrosamines and mortality from salivary gland cancer among rubber workers. *Epidemiology*, **10**, 786-7.
Sunny L, Yeole BB, Hakama M, et al. (2004). Oral cancers in Mumbai, India: a fifteen years perspective with respect to incidence trend and cumulative risk. *Asian Pac J Cancer Prev*, **5**, 294-300.
Swaminathan R, Selvakumaran R, Esmy PO, et al. (2009). Cancer pattern and survival in a rural district in South, India. *Cancer Epidemiol*, **33**, 325-31.
Swederlow AJ, Marmot MG, Grulich AE, et al. (1995). Cancer mortality in Indian and British ethnic immigrants from the Indian sub-continent to England and Wales. *Br J Cancer*, **72**, 1312-9.
Takiar R, Vijay CR (2011). An alternative approach to study the changes in the cancer. Pattern of men in India (1988-2005). *Asian Pac J Cancer Prev*, **12**, 875-8.
Tomatis L, Aitio A, Day NE, et al. (1990). Cancer: causes, occurrence and control. *IARC*, **100**, 1-368.
Tondon M, Kapil U, Bahadur S, et al. (2000). Role of micronutrients and trace elements in carcinoma of larynx. *J Assoc Physicians India*, **48**, 995-8.
Tsai CC, Chen CL, Hsu HC (1996). Expression of Epstein-Barr virus in carcinoma of major salivary glands: a strong association with lymphoepithelioma like carcinoma. *Hum Pathol*, **27**, 258-62,
Vaidya AD, Pantvaidya GH, Metgudmath R, et al. (2012). Minor salivary gland tumors of the oral cavity: a case series with review of literature. *J Cancer Res Ther*, **1**, 111-5.
Varma KD (1999). Thyroid cancer: Experiences at Uttar Pradesh. In: Thyroid Cancer - An Indian Perspective (ISBN-8187099054, 9788187099055), Eds. Shah D, Samuel AM, Rao RS. *Quest Publication*, 595.
WHO (2003). Concerted global action is the only answer to rising cancer deaths WHO 2003.
WHO-UICC (2003). Global Action Against Cancer, Publication of WHO (ISBN 92 4 1590726) 2003.
Wynder EL, Bross IJ, Day E (1956). Epidemiological approach to the etiology of the cancer of larynx. *JAMA*, **160**, 1384.
Yeole BB, Kurkure A, Advani S, et al. (2001). An assessment of cancer incidence patterns in parsi and non-parsi populations, greater Mumbai. *Asia Pac J Cancer Prev*, **2**, 293-8.
Yeole BB, Kurkure AP, Sunny L (2011). Cancer survival in Mumbai (Bombay), India, 1992-1999. *IARC Sci Publ*, **162**, 133-42.
Yoganathan P (2002). Betal chewing creeps into the new world, *NZ Dent J*, **98**, 40-5.
Yu MC (1991). Nasopharyngeal carcinoma: Epidemiology and dietary factors. *IARC Sci publication*, **105**, 39.
Zheng W, Shu XO, Ji BT, et al. (1996). Diet and other risk factors for cancer of the salivary glands: a population based case control study, *Int J Cancer*, **67**, 194-8.
Zinyu R, Kumar S, Dutta LP (1990). Studies on cancer of nasopharynx in Nagaland India. Proceedings of the XIV world congress of otorhinolaryngology and Head and Neck Surgery. Eds Sacriston T. Kugler and Ghedini Publications, Amsterdam 1990; pg 1279.